REMARKS

The Examiner has issued an Official Action requiring restriction between three groups of inventions. The groups identified by the Examiner are:

Group I: Claims 1-8, drawn to a plasmid construct;

Group II: Claims 9-14, drawn to a method for preparing and immobilising a protein on a support and

Group III: Claims 15 and 16, drawn to a two-component system.

Applicants respectfully traverse this restriction requirement.

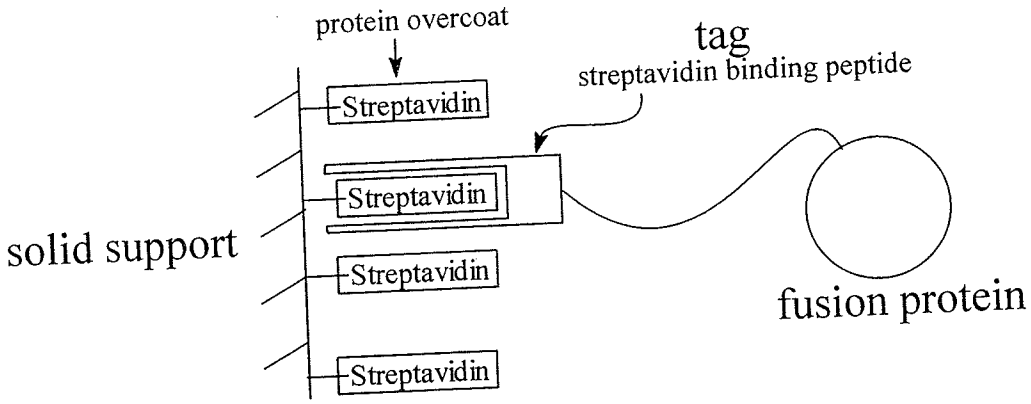
However, to expedite prosecution, the claims of Group I, namely claims 1-8 are provisionally elected.

The inventors note the Examiner's the comments concerning the Keefe et al. reference but respectfully disagree with the Examiner's conclusion that the claimed invention is not novel. The claimed invention differs technically from the prior art specified by Keefe et al. in that the plasmid construct of the invention features distinguishing fundamental elements:

1. Inherent flexibility to select a variety of tag-support interactions. Generality and ease of application are the strongest attributes of this invention. Different modes of interaction between tag and support can be conveniently tailored into the invention by selecting a tag sequence encoding peptides bearing various side-chains and a corresponding support bearing appropriately interactive surface groups. The potential list of available interactions is not restricted to a few specific examples and merely rests on intelligently anticipating suitable tags and surface groups to conveniently enable a certain application. In particular, the possible modes of non-covalent

interaction are inclusive but not limited to ionic, coordination, hydrophobic, dipolar, quadrupolar, and hydrogen bonding interactions. For instance, a poly-glu tag can be affixed to a positively-charged support. Equally plausible is a poly-phe tag affixed to a polystyrene support. Overall, the bond strength will reflect the combined contributions of many similar interactions or a weight-averaged contribution encompassing different modes of interaction. Hence the range of modes potentially amenable for use within the scope of the invention is notably broad as opposed to narrow. Even covalent interactions between tag and support surface can be employed by effecting a chemical reaction between tag and immobilized reactive groups positioned along a suitably designed support.

In contrast, emphasized in the prior art is a specific interaction between support-immobilized streptavidin and a streptavidin-binding tag bearing the specific peptide sequence of MDEKTTGWRGGHVVEGLAGELEQLRARLEHHPQGQREP. The mode of interaction between streptavidin and this laboriously-optimized tag may classify as a non-covalent "ligand-receptor binding interaction", a term that reflects the high specificity of the interaction and concomitant inflexibility of the tag design. Thus, the mode of interaction employed in the prior art is in fact inherently limiting as opposed to promoting generality. The limitations of the prior art extend beyond the scope of the tag in that even an essential streptavidin-immobilized support is defined in the prior art whereas the present invention does not require a biological element in the support. Furthermore, in the prior art the immobilized target proteins are eluted from the support by incubation with biotin, a procedure that potentially precludes the support from subsequent use, owing to the inseparable nature of biotin-streptavidin (Electrophoresis, 2005, 26, 501-10). In the invention, however, elution conditions are convenient and permit reuse.



2. Shape-indifferent interactions between tag and support promote strong bonding. The strength and number of interactions formed between tag and support in the invention are governed only by the chemical compatibility and number of bonding partners positioned along the tag and support. The interactions are not inherently shape-sensitive and bond formation does not require shape-complementarity between tag and support, unlike classic ligand-receptor examples. While the flexible tag can potentially conform to a specific shape such as that defined by a receptor site, this attribute is not a pre-requisite to realizing effective tag-support interactions. Rather, it is sufficient that the tag arranges itself arbitrarily along the general microtopology of any support in a manner that reflects the availability of surface-interacting groups. In sharp contrast, a streptavidin-biotin interaction describes one of the strongest shape-specific, non-covalent

interactions to exist between ligand and receptor. This exceptional ligand-receptor interaction realizes high binding stabilization energies and exemplifies an extreme case of host-guest shape complementarity optimized over evolutionary time. The impressive high affinity and strength of this tag-receptor interaction is cited as yielding a Kd of 4x10-5nM. Looking to the prior art, the interaction between peptide binding tag and streptavidin exemplifies a man-made analogue of the biotin-streptavidin interaction, with binding strength approximating a Kd of 2.5nM and tag displacement requiring the specific addition of biotin. In the invention, relatively shape-indifferent non-covalent interactions such as cationic-anionic and hydrophobic-hydrophobic interactions are comparatively much weaker and much more easily displaced by non-specific groups. The overall strength of such interactions comes from the collective action of numbers. Since no high-affinity features are engineered into tag or support, the strength of the tag-support interaction cannot originate from shape-complementarity as was depicted between a biologically evolved receptor and natural ligand or laboriously-engineered tag. Rather, the strength merely originates from realizing a large number of arbitrarily (and very likely sub-optimally) positioned, non-covalent interactions between tag and support surface. Covalent interactions can also contribute to the list of shape-indifferent interaction modes.

Therefore, the claimed invention is not anticipated by the Keefe et al. reference.

All rights to file one or more divisional applications directed to the subject matter of the nonelected claims and/or any other subject matter disclosed in the specification are preserved.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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